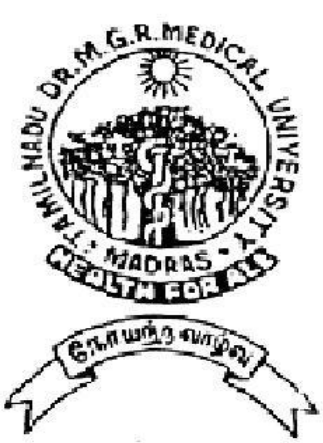
STUDY OF THYROID DYSFUNCTION IN SYSTEMIC LUPUS ERYTHEMATOSUS

Dissertation submitted for

MD Degree (Branch-I)

General Medicine



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APRIL – 2012

CERTIFICATE

This is to certify that this dissertation titled **"STUDY OF THYROID DYSFUNCTION IN SYSTEMIC LUPUS ERYTHEMATOSUS "** submitted by **DR.B.MADELINE VITHYA** to the faculty of General Medicine, The Tamil Nadu Dr.M.G.R. Medical University, Chennai in partial fulfillment of the requirement for the award of MD degree Branch I (General Medicine) is a bonafide research work carried out by her under our direct supervision and guidance.

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DECLARATION

I, **Dr.B. MADELINE VITHYA**, solemnly declare that the dissertation titled **'STUDY OF THYROID DYSFUNCTION IN SYSTEMIC LUPUS ERYTHEMATOSUS'** has been prepared by me.

This is submitted to the Tamil Nadu Dr.M.G.R. Medical University, Chennai in partial fulfillment of the requirement for the award of MD degree Branch I (General Medicine).

Place: Madurai

Date**:** **Dr. B. MADELINE VITHYA**

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ABBREVATIONS

SLE	**–**	**Systemic Lupus Erythematosus**
AITD	**–**	**Autoimmune Thyroid Disease**
AID	**–**	**Autoimmune Disease**
TPO	**–**	**Thyroid Peroxidase**
TPO Ab	**–**	**Thyroid Peroxidase Antibodies**
TSH	**–**	**Thyroid Stimulating Hormone**
TgAb	**–**	**Thyroglobulin antibodies**
T_3	**–**	**Triiodothyronine**
T_4	**–**	**Tetraidothyronine**
HLA	**–**	**Human Leukocyte Antigen**
RA	**–**	**Rheumatoid Arthritis**
SS	**–**	**Sjogrens Syndrome**
EUS	**–**	**Euthyroid sick syndrome**
NTI	**–**	**Non thyroidal illness**

STUDY OF THYROID DYSFUNCTION IN SYSTEMIC LUPUS ERYTHEMATOSUS

ABSTRACT

Background: The higher prevalence of thyroid dysfunction in systemic lupus erythematosus patients compared to that of normal population still remains a debatable issue.

Objective: To study the prevalence and pattern of thyroid dysfunction and thyroid antibodies in thirty five patients with Systemic Lupus Erythematosus admitted in our centre over two years.

Methods: Thirty five Systemic Lupus Erythematosus patients and twenty healthy subjects were evaluated by complete history and physical examination. Patients were assessed both clinically and biochemically for thyroid abnormalities.

Results: The prevalence of thyroid dysfunction (40%) in our study group was higher than that of the normal population (5%). Out of which, the prevalence of subclinical hypothyroidism (20%) was found to be significantly higher than that of the normal population while the prevalence of hyperthyroidism though higher in frequency was not significantly different from that of the normal population. Overall eleven out of thirty five patients (31.4%) were positive for thyroid

peroxidase antibodies with about four patients (36.36%) in this subgroup having thyroid dysfunction. Among the fourteen patients with thyroid dysfunction, four (28.57%) had autoimmune thyroid disease with subclinical hypothyroidism being the most common thyroid dysfunction.

Conclusion: Thyroid dysfunction in our study group was significantly higher with majority of patients having subclinical hypothyroidism. The prevalence of thyroid autoimmunity was also significantly high suggesting an ongoing slowly destructive autoimmune thyroiditis which could later manifest as overt thyroid dysfunction. Hence thyroid abnormalities are more common in systemic lupus erythematosus which may need regular monitoring to decrease the morbidity and improve the quality of life in this subset of patients.

Keywords: systemic lupus erythematosus, thyroid dysfunction, autoimmunity.

1. INTRODUCTION

Autoimmune diseases can be divided into organ specific and systemic illness. Some of the most common systemic inflammatory autoimmune diseases encountered in clinical practice include rheumatoid arthritis, systemic lupus erythematosus, dermatomyositis, polymyositis and systemic sclerosis. Autoimmune thyroid disease is one of the most common manifestations of organ specific autoimmune diseases. Whether concomitant organ specific and systemic autoimmune diseases occur more often by chance than expected is a controversial issue. Hence further studies are necessitated to establish this association.

Systemic lupus erythematosus is a disease of unknown etiology in which tissues and cells are damaged by pathological autoantibodies and immune complexes. Autoimmune thyroiditis is characterized by a slowly progressive asymptomatic phase followed later by complete destruction of the thyroid gland manifesting as overt hypothyroidism. Even though the demographic group at risk for SLE and autoimmune thyroid disease appears to be the same, there are several studies and case reports showing greater prevalence

of thyroid dysfunction in patients with SLE than the general population. Patients with SLE and coexisting thyroid dysfunction may escape clinical detection because of the similarities in clinical manifestations and the manifestations may be subtle, especially in the early stages of the disease. Treatment of the underlying thyroid dysfunction helps in improving the quality of life of the patient. Hence, although thyroid antibodies and thyroid disease are not included in the classification criteria for systemic lupus erythematosus, it is reasonable to explore whether patients with SLE have a higher prevalence of hypothyroidism and other thyroid diseases than that of the normal population.

2. REVIEW OF LITERATURE

2.1 BACKGROUND AND HISTORY:

Systemic lupus erythematosus (SLE) is an autoimmune disease in which organs and cells undergo damage mediated by tissue-binding autoantibodies and immune complexes[1]. It is frequently associated with other autoimmune diseases and autoantibodies. The most prevalent autoimmune disease found was Sjogren syndrome followed by rheumatoid arthritis, autoimmune thrombocytopenia and hypothyroidism[2]. The association between systemic lupus erythematosus (SLE) and thyroid abnormalities was first described in 1961 by White et al[3] and Hijmans et al[4], who showed that the presence of thyroid disturbances appeared to be more frequent in SLE patients than in the general population. Since then many series have been reported. The exact prevalence of thyroid diseases among South Indian population with SLE still remains unknown.

2.2 AUTOIMMUNITY AND AUTOIMMUNE DISEASE:

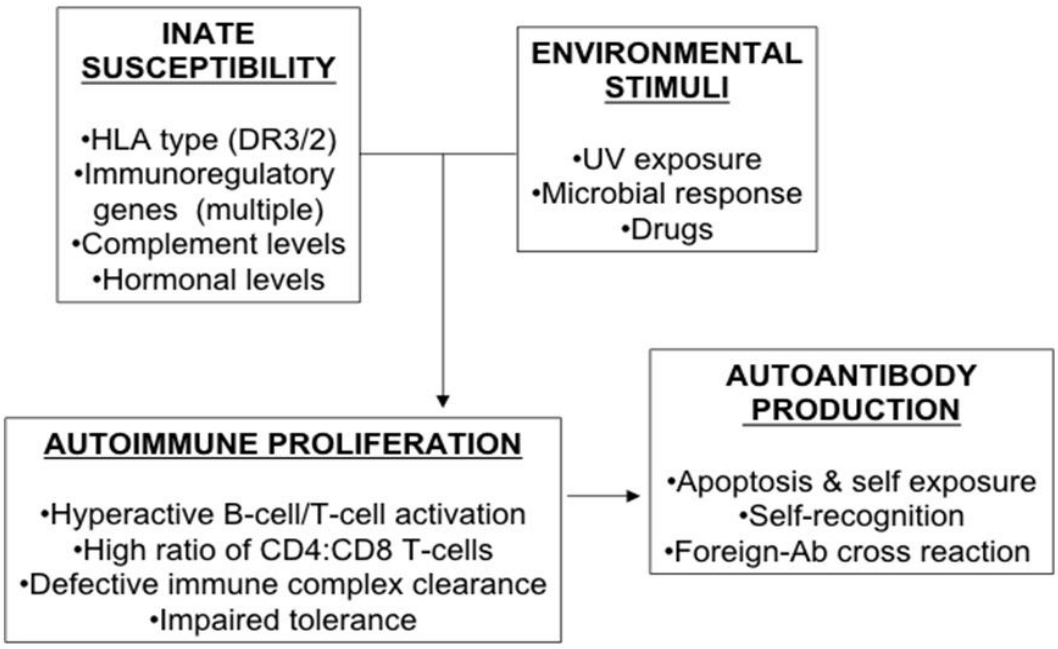
Autoimmunity leads to recognition of self antigens due to the breakdown of one or more of the basic mechanisms regulating

immune tolerance[5]. Autoimmune disease is that tissue injury is caused by the immunologic reaction of the organism with its own tissues. Autoimmunity, on the other hand, refers to the presence of antibodies or T lymphocytes that react with self-antigens and does not necessarily imply that the development of self-reactivity has pathogenic consequences[5].

In patients with systemic autoimmune diseases, the pathological lesions are found in multiple diverse organs and tissues whereas in organ specific autoimmune disease the manifestations are localized. SLE is a disease of protean manifestations that can be associated with a variety of autoimmune diseases. Demonstration of associated relevant autoimmune manifestations is likely to be etiologic in the organ pathology. The occurrence of common features of autoimmune diseases and the co association of multiple autoimmune diseases in the same individual or family support the notion that there may be common genetic factors that predispose to autoimmunity[6]. A sex ratio other than 1 in autoimmune disease is common, with women representing 75% of autoimmune patients[7].

2.3 SYSTEMIC LUPUS ERYTHEMATOSUS

SLE is a chronic, relapsing, inflammatory, and often febrile multisystemic disorder of connective tissue, characterized principally by involvement of the skin, joints, kidneys, and serosal membranes[8]. Ninety percent of patients are women of child-bearing years. Interactions between susceptibility genes and environmental factors result in abnormal immune responses[1]. The abnormal immune response that permits persistence of pathogenic B and T cells has multiple components that include processing of increased quantities of self antigens by antigen-presenting cells, hyperactivation of T and B cells, and failure of multiple regulatory networks to interrupt this process[8].



In the early stages of the disease, the signs may be subtle or non-specific. Systemic symptoms particularly fatigue, myalgias and arthralgias are present most of the time. SLE occurs 10 times more commonly in women than in men. The diagnosis of SLE is based on characteristic clinical features and autoantibodies (ACR 1997 criteria). Survival in patients with SLE is approximately 95% at 5 years, 90% at 10 years, and 78% at 20 years with treatment[1].

The current sine qua non of established lupus is the ANA test which is positive in more than 95% of patients at diagnosis. Although highly specific, anti-ds-DNA is not necessarily highly sensitive for lupus, nor is it always predictive of disease activity. Antibodies to Smith are also specific for SLE and do not usually correlate with disease activity or clinical manifestations. In addition to these, a number of specific epitopes within the nucleus have been shown to give rise to positive test results in lupus patients.

TABLE 2.1 AUTOANTIBODIES IN SYSTEMIC LUPUS ERYTHEMATOSUS(SLE)			
ANTIBODY	**PREVALENCE%**	**ANTIGEN**	**CLINICAL UTILITY**
ANA	98	Multiple nuclear	Best screening test
Anti – ds DNA	70	DNA(double stranded)	High titers are specific. Correlates with disease activity
Anti – Smith	25	Protein complexed to U1 RNA	Specific for SLE
Anti – RNP	40	Protein complexed to U1 RNA (gamma)	Overlap syndromes
Anti – Ro(SS-A)	30	Protein complexed to hY RNA (60 kDa)	Siccasyndrome. Predisposes to SCLE , neonatal lupus
Anti – La(SS-B)	10	Protein complexed to hY RNA (47 kDa)	Decreased risk for nephritis
Antihistone	70	Histones associated with DNA	Drug induced lupus
Antiphospholipid	50	Phospholipids, prothrombin	ELISA for cardiolipin, beta$_2$G1 and DRVVT
Antierythrocyte	60	Erythrocyte membrane	Overt hemolysis
Antiplatelet	30	Surface and altered cytoplasmic antigens on platelets	Thrombocytopenia
Antineuronal	60	Neuronal and lymphocyte surface antigens	Active CNS Lupus (CSF)
Antiribosomal P	20	Protein in ribosomes	Active CNS Lupus (serum)

Courtesy - Harrison’s textbook of internal medicine, seventeenth edition

2.4 SLE AND OTHER AUTOIMMUNE DISEASES

The association of systemic lupus erythematosus (SLE) with other autoimmune diseases (AID) is well established[4]. Interestingly, J E McDonagh, D A Isenberg et al reported that clustering of both systemic and organ specific autoimmune diseases (AID) occurs in patients with SLE with almost a third of patients having at least one other AID (30%)[2]. The association of additional AID in SLE patients is likely to be multifactorial with interplay of ubiquitous environmental and hormonal factors in genetically predisposed people. Hence, all patients with SLE should be screened for the possible development of a second AID during follow up and regular serological testing may be advantageous.

According to a study by S A Chambers, S C Charman et al, out of 401 patients with SLE, there were 131 patients (33% of the cohort) who had at least one other AID, including 100 (25%) with one other AID, 26 (7%) with two and 5 (1%) with three AID in addition to SLE[9]. Chronology of AID development in patients with SLE differs depending on the disease involved. Those patients whose additional AID was autoimmune thyroid disease were more likely to

develop this before SLE (75%) compared to 7% in the same year as diagnosis of SLE and 18 % after SLE[9].

The tendency for familial clustering of autoimmune diseases is well known. Studies of families with multiple autoimmune diseases have led to interesting discoveries that genetic factor that could play a vital role in the explanation of this phenomenon. One such discovery is the recognition of a single nucleotide polymorphism (rs2476601, encoding R620W) in the intracellular tyrosine phosphatase (PTPN22) that could confer risk of four separate autoimmune phenotypes (type 1 diabetes, rheumatoid arthritis, SLE and Hashimoto's thyroiditis) in the families that were studied[10]. This finding suggests a common underlying etiologic pathway for some autoimmune disorders.

In conclusion, patients with SLE might present with a variety of other AID and this could have an impact on damage and mortality[9]. Strategies for managing lupus patients who have additional AID should include close monitoring for the adverse effects associated with the prolonged use of higher doses of corticosteroids and other immunosuppressants that might be required to treat the combined autoimmune disorders.

2.5 AUTOIMMUNE THYROID DISEASE (AITD)

AITD is the most common organ specific autoimmune disorder comprising of Graves disease, Hashimoto's thyroiditis, atrophic thyroiditis, post partum thyroiditis, silent thyroiditis and thyroid associated ophthalmopathy[11]. It is a known fact that there is a higher prevalence of AITD in patients with other autoimmune diseases. These disorders share antibodies against thyroglobulin (Tg Ab), thyroid peroxidase (TPO Ag) and TSH receptor (TSH-R Ab) besides some other minor antigens[12]. Females are found to be commonly affected and this is due to sex steroid effects on the immune response. An X chromosome–related genetic factor may also contribute, which may account for the high frequency of autoimmune hypothyroidism in Turner syndrome. The concordance rate in monozygotic twins is 33-55% as compared to less than 5% in dizygotic twins. Autoantibody status, ultrasonographic features and fine needle aspiration biopsy findings are very useful in the diagnosis of AITD[13].

Patients may present with a goiter (Hashimoto's thyroiditis) or at the later stages of the disease (atrophic thyroiditis) goiter may not be

present. The autoimmune process gradually reduces thyroid function leading to a phase of compensation when normal thyroid hormone levels are maintained by a rise in TSH called subclinical hypothyroidism[14]. As the disease progresses, unbound T_4 levels fall and TSH levels rise further leading to clinical or overt hypothyroidism. The mean annual incidence rate is up to 4 per 1000 women and 1 per 1000 men. Japanese population is more commonly affected probably because of genetic factors and chronic exposure to a high-iodine diet. The mean age at diagnosis is 60 years, and the prevalence of overt hypothyroidism increases with age[14].

HLA-DR polymorphisms are the best documented genetic risk factors for autoimmune hypothyroidism, especially HLA-DR3, -DR4, and -DR5 in Caucasians. A weak association also exists between polymorphisms in *CTLA-4*, a T cell–regulatory gene, and autoimmune hypothyroidism. These genetic associations are not unique to autoimmune thyroid disease being also found in other autoimmune diseases. The onset is usually insidious, and the patient may become aware of symptoms only when euthyroidism is restored. Patients with Hashimoto's thyroiditis in the early stages

may be asymptomatic except for the presence of a goiter. On the contrary, patients with atrophic thyroiditis or the late stage of Hashimoto's thyroiditis may present with symptoms and signs of hypothyroidism[14].

Therefore, estimation of thyroid autoantibodies and TSH, T_3, T_4 are useful in the diagnosis of AITD[13]. Once clinical or subclinical hypothyroidism is confirmed, the etiology can be easily established by demonstrating the presence of TPO antibodies, which are present in >90% of patients with autoimmune hypothyroidism[14].Fine needle aspiration biopsy is very much useful in the diagnosis of AITD[12]. Thyroid ultrasonography could be useful for diagnosis especially in children where antibodies and biopsy are not feasible[15].

The prevalence rates according to several studies show that subclinical hypothyroidism is found in 6–8% of women and 3% of men. The annual risk of developing clinical hypothyroidism is about 4% when subclinical hypothyroidism is associated with positive TPO antibodies. On follow up, it is important to confirm that any elevation of TSH is sustained over a 3-month period in order to make future therapeutic decisions. As long as excessive treatment is

avoided, there is no risk in correcting a slightly increased TSH due to increased risk of progression to overt hypothyroidism. Treatment is administered by starting with a low dose of levothyroxine (25–50 g/d) with the goal of normalizing TSH[14].

2.6 THYROID AUTOIMMUNITY–THYROID SPECIFIC AUTOANTIBODIES

Antibodies against thyroid specific antigens, anti-thyroid peroxidase (TPO), thyroglobulin (Tg), and TSH receptors are useful in the diagnosis of autoimmune thyroid disorders.

Thyroid peroxidase enzyme (TPO) was recently discovered to be the principal antigen in the thyroid microsomes.TPO is an useful enzyme in the biosynthesis of thyroid hormones and catalyses the oxidation of an iodide ion and the coupling of iodotyrosyl residues of Tg. Patients with Grave's disease, Hashimoto's, atrophic thyroiditis or post-partum thyroiditis have all been known to be TPO Ab positive. Thyroid peroxidase antibodies have been implicated to be a cytotoxic agent associated with the destructive process involved in the hypothyroidism seen with autoimmune thyroiditis. Several

studies have indicated that these antibodies usually precede the development of thyroid dysfunction. Future studies may even indicate that it can be used as a prognostic indicator for thyroid dysfunction. The paradoxical absence of TPOAb in some patients with unequivocal TSH abnormalities likely reflects the suboptimal sensitivity or specificity of current TPOAb tests or non autoimmune thyroid failure (atrophic thyroiditis)[16].

TPOAb is also detected at higher levels in patients with non-thyroid autoimmune diseases such as type 1diabetes and pernicious anemia. Euthyroid patients with detectable TPOAb are at an increased risk for development of hypothyroidism. Detectable level of TPOAb typically precedes the development of an elevated TSH and is therefore considered to be a risk factor for hypothyroidism. Apart from hypothyroidism, the presence of TPO Ab is associated with reproductive complications such as miscarriage, infertility, IVF failure, fetal death, pre-eclampsia, preterm delivery and post-partum thyroiditis. Depression is also associated with increased levels of TPOAb. The enhanced sensitivity and specificity of the TPO immunoassay methods make them a more cost-effective option over the older semi-quantitative AMA agglutination tests, since they

obviate the need for additional TgAb measurements in the routine diagnosis of autoimmune thyroid disorders[16].

Thyroglobulin autoantibodies (TgAb) are also found in autoimmune thyroid conditions, usually in association with TPOAb. However, the recent NHANES III study found that only 3 % of subjects with no risk factors for thyroid disease had isolated elevation of thyroglobulin antibodies and there was no association with TSH abnormalities. Therefore the clinical significance of an isolated TgAb abnormality remains to be established. This study suggests that it is unnecessary to measure both TPOAb and TgAb for a routine evaluation of thyroid autoimmunity[16]. TSH Receptor antibodies are useful in the differential diagnosis of hyperthyroidism, the prediction of fetal and neonatal thyroid dysfunction due to transplacental passage of maternal TRAb and prediction of the course of Graves' disease treated with anti thyroid drugs[16] but not for the diagnosis of autoimmune thyroiditis.

The prevalence of anti TPO antibodies and TgAb is high in SLE patients than in controls, although their inhibitory activity is less than in thyroid diseases[17].On analyzing several studies, antibodies to other thyroid antigens have been only rarely assayed in

SLE. Thyroid stimulating immunoglobulin / thyroid binding inhibitory immunoglobulin, both of which target the TSH receptor have been found in the sera of 5 and 10 of 28 SLE patients[18]. Hence the routine testing for these antibodies are not necessary.

2.7 AITD AND SYSTEMIC AUTOIMMUNE DISORDERS

Autoimmune hypothyroidism may be associated with signs or symptoms of other autoimmune diseases, particularly vitiligo, pernicious anemia, Addison's disease, alopecia areata, and type 1 diabetes mellitus. Less-common associations include celiac disease, dermatitis herpetiformis, chronic active hepatitis, rheumatoid arthritis, systemic lupus erythematosus (SLE), and Sjögren's syndrome. The association of chronic autoimmune thyroiditis with rheumatic diseases such as systemic lupus erythematosus (SLE), Sjögren's syndrome (SS), systemic sclerosis, rheumatoid arthritis (RA) is well recognized[4,17,19-22].This result suggests extensive genetic sharing among these autoimmune diseases. Many rheumatic manifestations such as fibrositis, myositis, myalgias, carpal tunnel syndrome, joint stiffness, and joint effusion have been described in

association with chronic autoimmune thyroiditis and these symptoms seem to be due to hypothyroidism which is frequently seen[23,24].

2.8 THYROID DISEASES IN SYTEMIC LUPUS ERYTHEMATOSUS

A number of studies have suggested that thyroid disease is more common in SLE than in the general population, but there is disagreement as to whether both hypothyroidism and hyperthyroidism are more common or whether this finding is restricted to hypothyroidism alone. Both antithyroglobulin and antimicrosomal antibodies have been found with greater frequency in SLE than in the general population, even in lupus patients who do not have clinical thyroid disease[25,26]. It is still a subject of discussion as to whether SLE is an independent risk factor for these thyroid abnormalities or whether this is a coincidental finding because the group most at risk for SLE, young to middle aged women, is precisely the same group most at risk for autoimmune thyroid disease[27].

Analyzing the frequency of AID by ethnic group, it was found that among the South Asians, 13 (76.5%) had one AID, 3 (17.6%)

had two and 1 (5.9%) had three other AID. In South Asians, autoimmune hypothyroidism was the most common other AID (27.3%) followed by Sjogrens syndrome (22.7%), antiphospholipid syndrome and myositis[9]. Subgroup analysis revealed that a higher proportion of South Asians developed thyroid disease compared to the black patients[9]. Attia and colleagues examined the occurrence of other AID in 60 Arab and Asian patients from the Indian subcontinent with SLE under follow-up for 12 years in Abu Dhabi and reported similar findings[28].The R620W polymorphism of the *PTPN22* gene appears to be a risk factor for concurrent autoimmune thyroid disease and SLE[29]. The locus 5q14.3-15 harbors a susceptibility gene which may be shared by SLE and AITD[49].Also stratifying SLE pedigrees by the presence of other autoimmune disorders may facilitate the discovery of other genes related to SLE.

In summary it is clear that SLE and other AID coexist commonly in individual patients. It is important to be aware of this, because symptoms of different AID can often be very similar, which means that diagnosis of a second AID could potentially be delayed

by wrongful attribution of symptoms to the first. Hence the need for additional testing of associated thyroid dysfunction.

2.9 PREVALENCE OF AITD IN SYSTEMIC LUPUS ERYTHEMATOSUS

TABLE 2.2: Studies of the prevalence of hyperthyroid and hypothyroid disease in SLE

STUDY	NO : SLE	NO: HYPO THYROID	% OF HYPO THYROIDISM	NO: HYPER THYROIDISM	% OF HYPER THYROIDISM
Bryon et al[31.]	64	3	4.7	7	10.9
Weetman et al[32.]	41	10	24	0	0
Chang et al[33.]	45	2	4.4	1	2.2
Boey et al[34.]	129	5	3.9	1	0.8
Vianna et al[35.]	100	6	6	2	2
Eberhad et al[36.]	35	4	11.4	0	0
Miller et al[37.]	332	22	6.6	3	0.9
Kohner et al[38]	175	9	5	0	0
Rodrique et al[39]	93	--	--	6	6.5

Two studies have suggested that there is no statistically significant difference in the prevalence of thyroid disease in SLE compared with age and sex matched controls, despite a higher prevalence of antithyroglobulin antibodies being found in the SLE group[3,5]. Because only a few studies have examined this issue, and numbers were small, the question as to whether lupus patients have

an excess of thyroid disease over and above that of age and sex matched controls remains debatable.

Despite this, the reported prevalence of autoimmune thyroid disease (3.9–24%) and antithyroid antibodies (11–51%) in SLE varies considerably from different studies. High risk patients especially females, raised TSH, positive TPO antibodies should have thyroid function follow up and should be given thyroid treatment in due course. Therefore it is recommended to perform intermittent biochemical screening of thyroid function in patients with SLE, particularly if they are known to have thyroid antibodies, to identify clinical/subclinical thyroid disease.

3. AIM AND OBJECTIVES

The aim of the study were as follows

1. To study the prevalence and pattern of thyroid dysfunction in Systemic lupus erythematosus patients.
2. To determine the prevalence of thyroid autoimmunity among them.
3. To correlate thyroid autoimmunity with thyroid dysfunction.
4. To correlate any age, gender and disease duration difference among SLE patients with and without thyroid dysfunction.

4. MATERIALS AND METHODS.

STUDY DESIGN

Cross sectional observational study to analyze the prevalence of thyroid disorders and thyroid autoimmunity among Systemic lupus erythematosus patients.

SETTING

Collaborating departments:

Department of Medicine/ Department of Endocrinology/ Division of Rheumatology, Government Rajaji Hospital, Madurai Medical College, Madurai.

APPROVAL

The study was approved by the ethical committee of Government Rajaji Hospital, Madurai Medical College.

STUDY POPULATION

Systemic lupus erythematosus patients who attended the Department of Rheumatology and Department of Medicine from April 2010 to September 2011 were enrolled in the study along with appropriate age and sex matched controls. Thirty five patients among them satisfied criteria for inclusion into the study. Twenty

age and sex matched people from normal population were taken as controls.

No. of patients enrolled : 35

No. of controls : 20

INCLUSION CRITERIA

Established cases of SLE as per the American college of Rheumatology criteria 1982(revised in 1997)

EXCLUSION CRITERIA

1. Pregnancy
2. Evidence of other autoimmune diseases like Addison's disease, vitiligo, autoimmune hepatitis, rheumatoid arthritis.
3. Chronic kidney disease
4. Past history of thyroid surgery or radioiodine therapy
5. Critically ill patients.
6. Patients taking drugs which alter thyroid function tests.

CONSENT

Patients were informed about the details of the test performed and blood sample collected with consent.

SAMPLE COLLECTION

Venous blood sample was collected. After serum separation, sample was sent for analysis.

METHOD OF TESTING

T_3 , T_4 , TSH – chemiluminescence immunoassay(CLIA)

TPO – Enzyme chemiluminescence immunoassay (ECLIA)

NORMAL RANGE

T_3 – 80 – 200 ng/dl

T_4 – 4.6 – 13 µg/dl

TSH 3rd generation(hs TSH) – 0.27 – 4.20 mIu/mL

Anti TPO Ab – 0-34 IU/L

INTERPRETATION OF RESULTS

NO	T_3	T_4	TSH	ANTI TPO Ab	INTERPRETATION
1	N	N	N	N	Euthyroidism
2	N	N	Increased (up to 10 mIu/L)	N	Subclinical hypothyroidism
3	Decreased	Decreased	Increased (>10 mIu/L)	N	Overt hypothyroidism
4	N	N	Decreased	N	Subclinical hyperthyroidism
5	Increased	Increased	Decreased	N	Hyperthyroidism
6	Decreased	N/ Decreased	Variable	N	Non thyroidal illness(ESS)
7	Variable	Variable	Variable	Positive	Thyroid autoimmunity
8	Hypothyroidism or hyperthyroidism with positive anti TPO Ab				Autoimmune thyroid disease

STATISTICAL ANALYSIS

The information collected regarding all the selected cases were recorded in a Master Chart. Data analysis was done with the help of computer using **Epidemiological Information Package (EPI 2010)** developed by Centre for Disease Control, Atlanta.

Using this software range, frequencies, percentages, means, standard deviations, chi square and 'p' values were calculated. Kruskul Wallis chi-square test was used to test the significance of difference between quantitative variables and Yate's chi square test for qualitative variables. A 'p' value less than 0.05 is taken to denote significant relationship.

5. RESULTS AND ANALYSIS OF OBSERVED DATA

Total number of patients enrolled in the study : 35

Number of males : 3

Number of females: 32

Number of patients with thyroid dysfunction : 14 out of 35 (40%)

1. No of subclinical hypothyroid patients : 7 out of 35 (20%)
2. No of overt hypothyroid patients : nil
3. No of hyperthyroid patients : 4 out of 35(11.4%)
4. No of patients with ESS : 3 out of 35(8.6%)

Number of patients with positive

Anti TPO Antibodies : 11 out of 35 (31.4%)

1. Euthyroidism : 7 out of 11(63.63%)
2. Subclinical hypothyroidism : 3 out of 11(27.27%)
3. Hyperthyroidism : 1 out of 11(9.09%)

Number of patients with thyroid dysfunction and positive Anti TPO Antibodies: 4 out of 35 (11.42%)

1. Subclinical hypothyroidism : 3 out of 4 (75%)
2. Hyperthyroidism : 1 out of 4 (25%)

Prevalence of autoimmune thyroid disease in patients with thyroid autoimmunity : 4 out of 11 (36.36%)

Total number of controls enrolled in the study : 20

Number of males : 3

Number of females : 17

Number of patients with thyroid dysfunction : 1 out of 20 (5%)

Number of patients with thyroid : 1 out of 20 (5%)

Autoimmunity

Number of patients with AITD : Nil

ANALYSIS OF OBSERVED DATA

PROFILE OF CASES STUDIED:

TABLE 1

AGE DISTRIBUTION OF STUDY AND CONTROL GROUP

Age group	Study group		Control group	
	No	%	No	%
< 20 years	5	14.3	5	25
20-29 years	20	57.1	5	25
30-39 years	8	22.9	9	45
40 & Above	2	5.7	1	5
Total	35	100	20	100
Range	16-52 years		15-40 years	
Mean	26.3 years		27.7 years	
SD	8.0 years		7.9 years	
'p'	0.3352 Not significant			

The age of the study group was 26.3 $\pm$8 years and the control group was 27.7 $\pm$7.9 years. The difference is not statistically significant (p = 0.3352).

CHART 1 : MEAN AGE DISTRIBUTION OF THE STUDY AND CONTROL **GROUP**

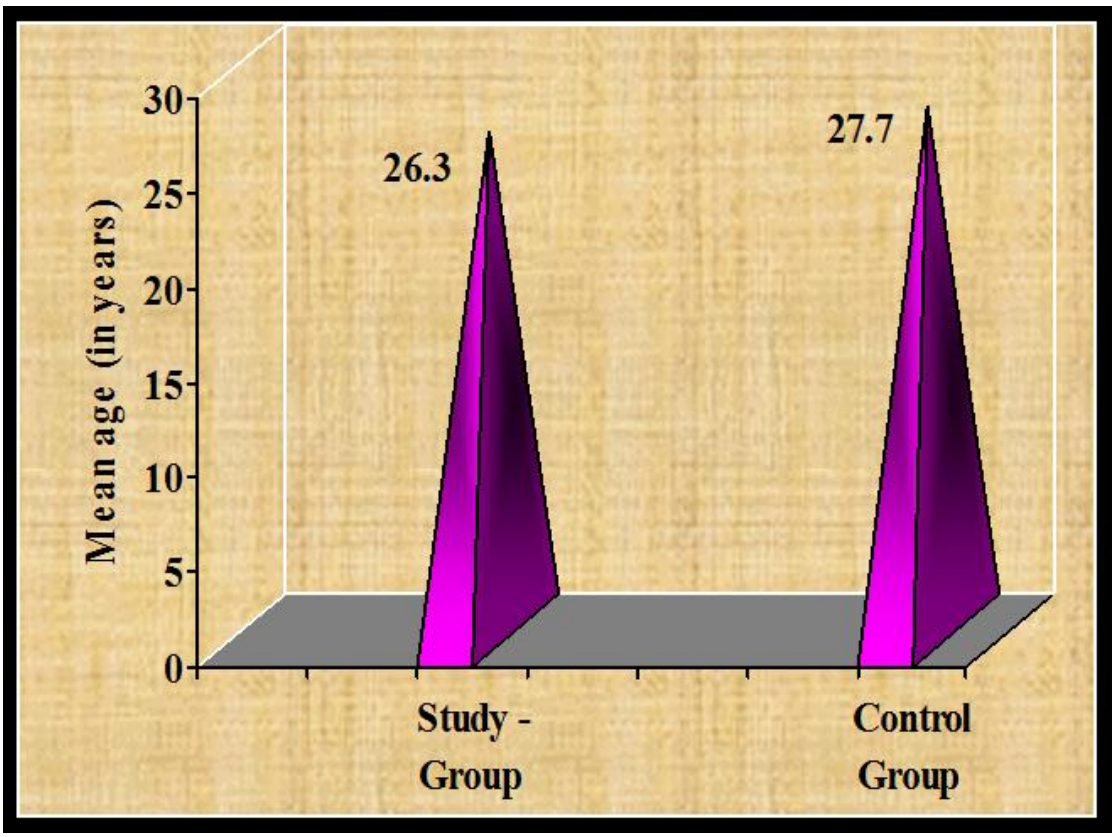


TABLE 2

SEX DISTRIBUTION OF STUDY GROUP AND CONTROL GROUP

Sex	**Study group**		**Control group**	
	No	**%**	**No**	**%**
Male	3	8.6	3	15
Female	32	91.4	17	85
Total	35	100	20	100
'p'	0.3769 Not significant			

91.4 % of the study group and 85% of the control group were females. The difference in the sex composition is not significant ($p > 0.05$).

CHART 2: MEAN SEX DISTRIBUTION OF STUDY AND CONTROL GROUP

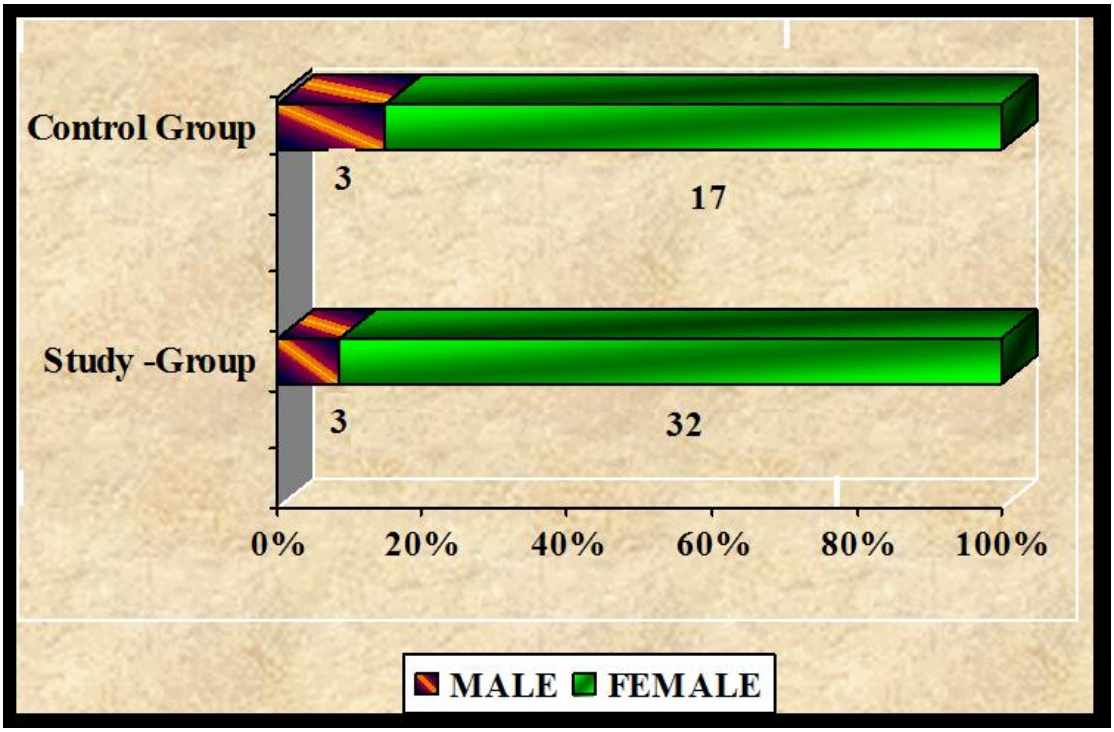


TABLE - 3

THYROID DYSFUNCTION IN STUDY AND CONTROL GROUP

Interpretation	**Study group**		**Control group**	
	No	**%**	**No**	**%**
Euthyroid Non thyroidal illness	21 3	60 8.6	19 1	95 5
Subclinical hypothyroidism Hyperthyroidism	7 4	20 11.4	- -	- -
Total	35	100	20	100
'p'	**0.0051** **Significant**			

Thyroid dysfunction was present in 40% of the study cases and in 5% of the control cases and the difference is found to be statistically significant ($p<0.0051$)

CHART 3 COMPARISON OF THYROID STATUS IN STUDY AND CONTROL POPULATION.

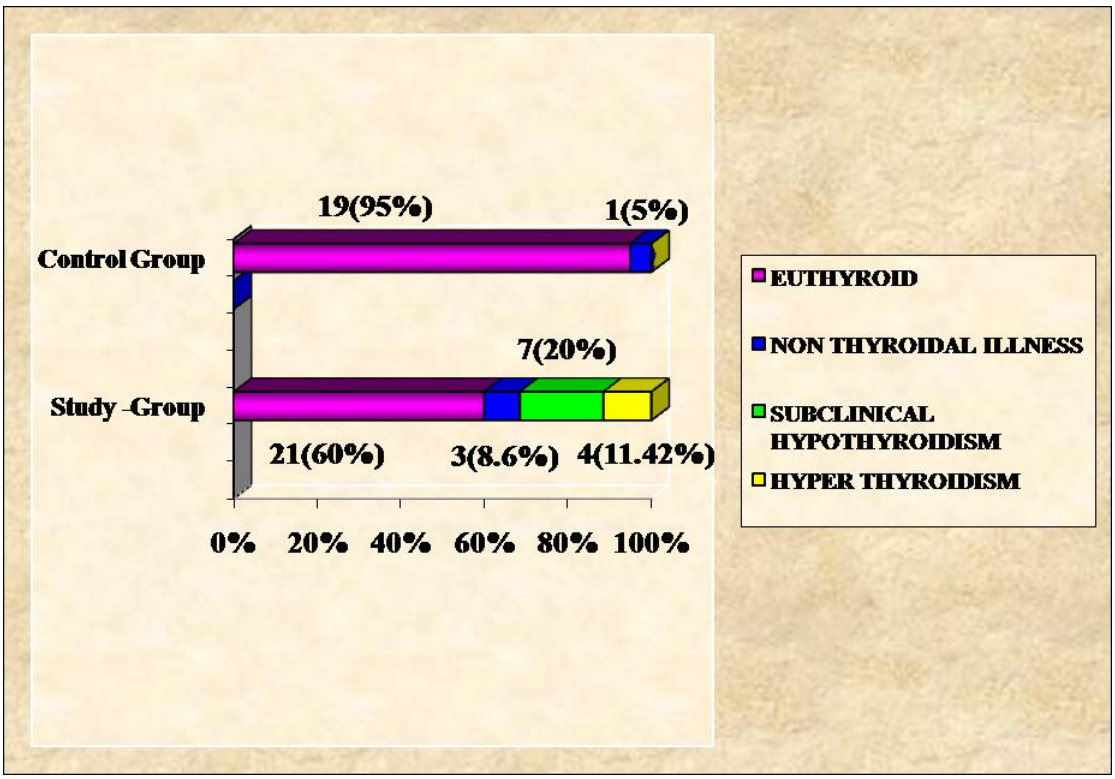


CHART 4: THYROID STATUS OF PATIENT POPULATION IN PERCENTAGE

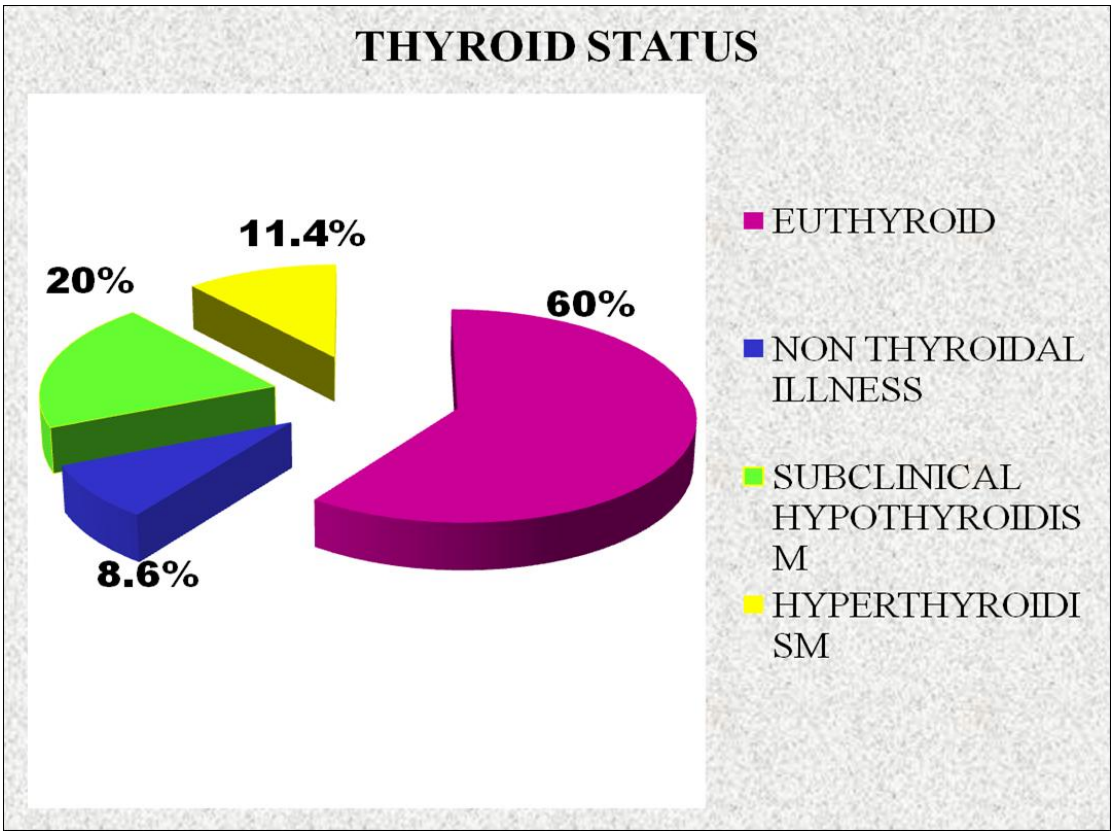


TABLE 4

THYROID STATUS IN RELATION TO AGE

Thyroid dysfunction	**Age (in years)**	
	Mean	**SD**
Yes	24.2	6.4
No	27.2	8.5
‘p’	0.2772 Not significant	

There was no significant relationship between thyroid dysfunction and age of the patient.

CHART 5: THYROID STATUS IN RELATION TO AGE

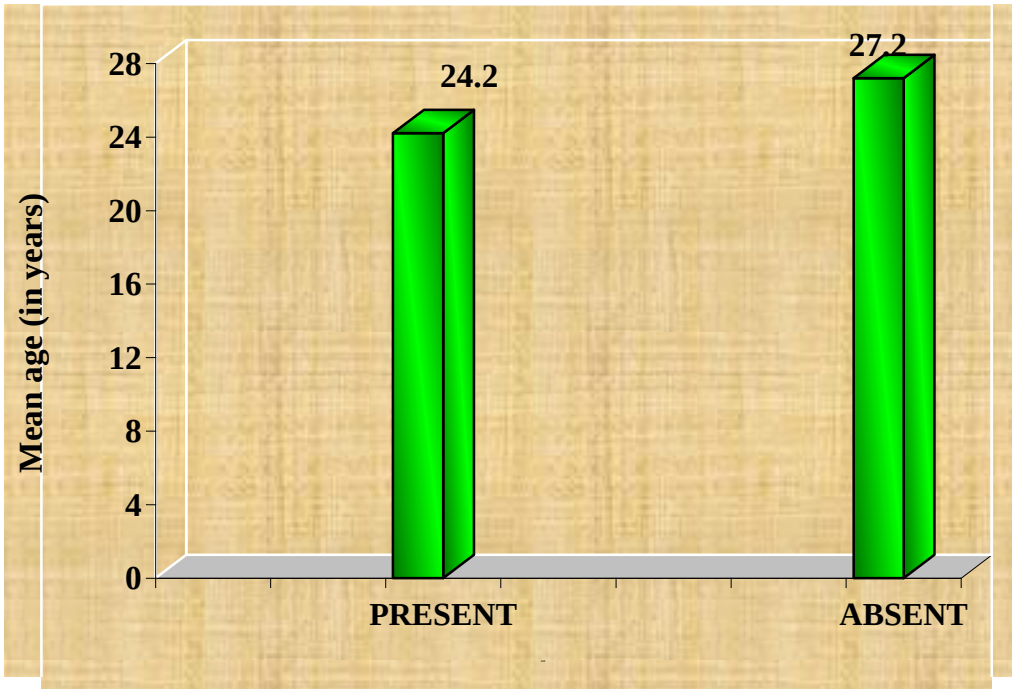


TABLE 5

THYROID DYSFUNCTION IN RELATION TO SEX

Sex	**No .of cases**	**Thyroid dysfunction**			
		Yes		**No**	
		No	**%**	**No**	**%**
Male	3	2	66.66	1	33.33
Female	32	11	34.37	21	65.62
'p'	0.227 Not significant				

Sex of the patient and incidence of thyroid disease were not significantly related ($p > 0.05$).

CHART 6: THYROID DISEASE IN RELATION TO SEX

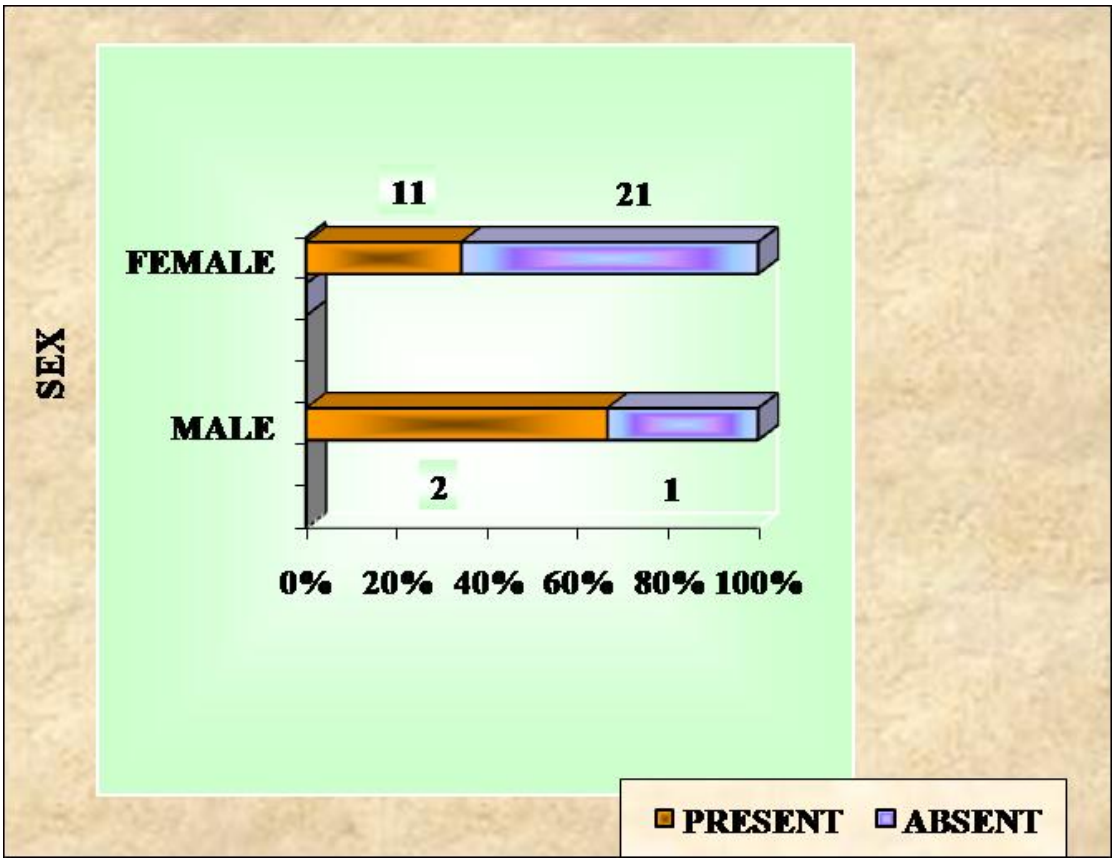


TABLE 6

THYROID STATUS IN RELATION TO

DURATION OF DISEASE

Thyroid dysfunction	Duration in years	
	Mean	SD
Yes	1.21	1.86
No	1.49	2.18
'p'	0.4383 Not significant	

Duration of illness did not have any significant relationship with incidence of thyroid dysfunction.

CHART 7: THYROID STATUS IN RELATION TO DURATION OF DISEASE

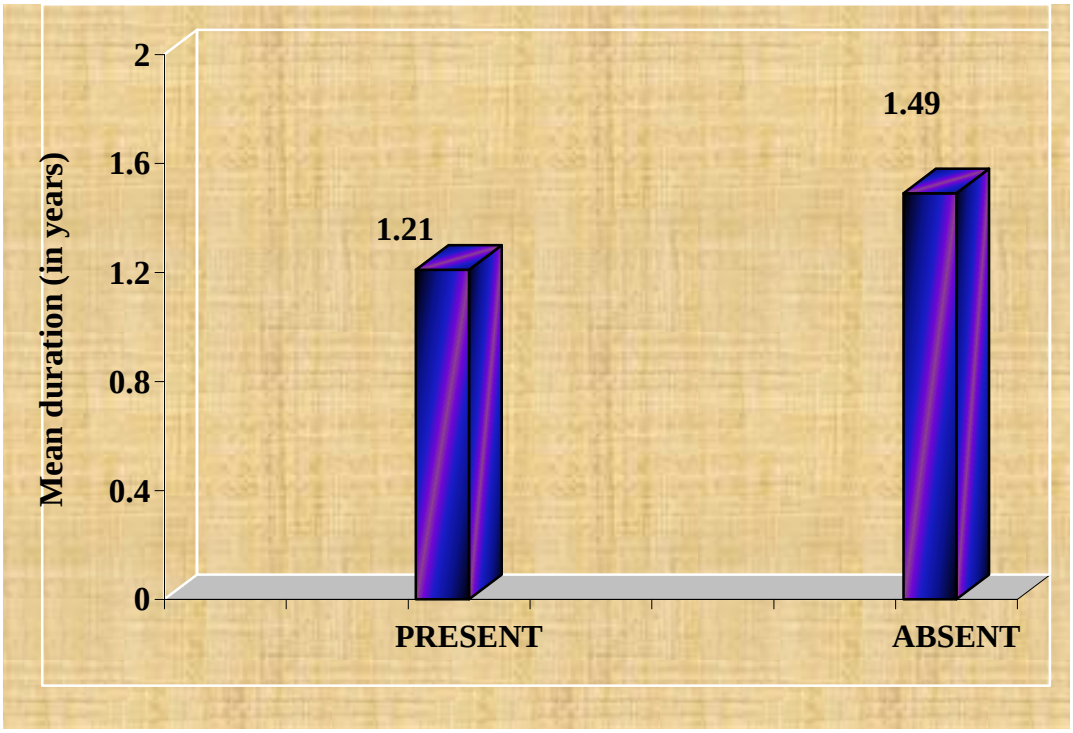


TABLE 7

THYROID STATUS IN RELATION TO

SYMPTOMATOLOGY

Symptoms	**No. of cases**	**Thyroid dysfunction**			
		Yes		**No**	
		No	**%**	**No**	**%**
Present	16	6	37.5	10	62.5
Absent	19	8	42.10	11	57.89
'p'	0.7304 Not significant				

Presence or absence of symptoms did not significantly affect incidence of thyroid dysfunction (p = 0.7304).

TABLE 8

SUBCLINICAL HYPOTHYROIDISM IN STUDY AND CONTROL POPULATION

SUBCLINICAL HYPOTHYROIDISM	Study group		Control group	
	No	**%**	**No**	**%**
Yes	7	20	0	0
No	28	80	20	100
'p'	**0.0331 Significant**			

Subclinical hypothyroidism was present in 20% of study cases and none of control cases. This difference is statistically significant (p = 0.0331).

CHART 8: SUBCLINICAL HYPOTHYROIDISM IN STUDY AND CONTROL POPULATION

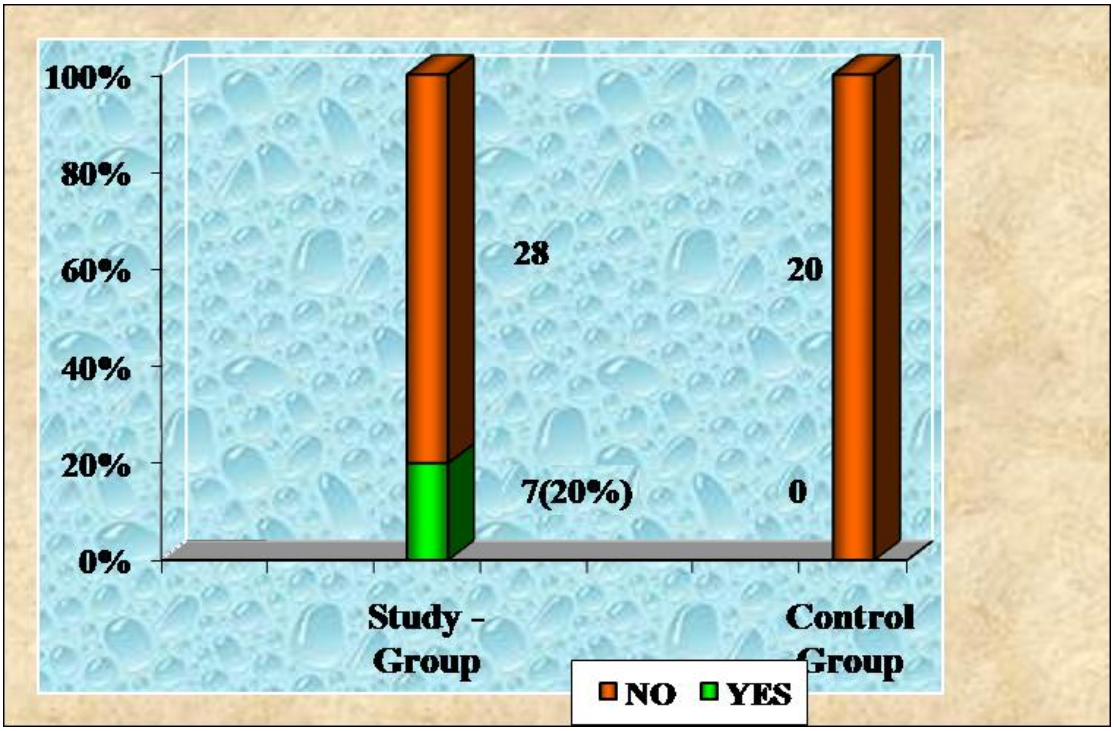


TABLE 9

HYPERTHYROIDISM IN STUDY AND CONTROL POPULATION

HYPER THYROIDISM	Study group		Control group	
	No	**%**	**No**	**%**
Yes	4	11.42	0	0
No	31	88.57	20	100
'p'	**0.1535 Not Significant**			

Hyperthyroidism was present in 11.42% of study cases and none of control cases. This difference is not statistically significant (p = 0.1535).

CHART 9 : HYPERTHYROIDISM IN STUDY AND CONTROL POPULATION

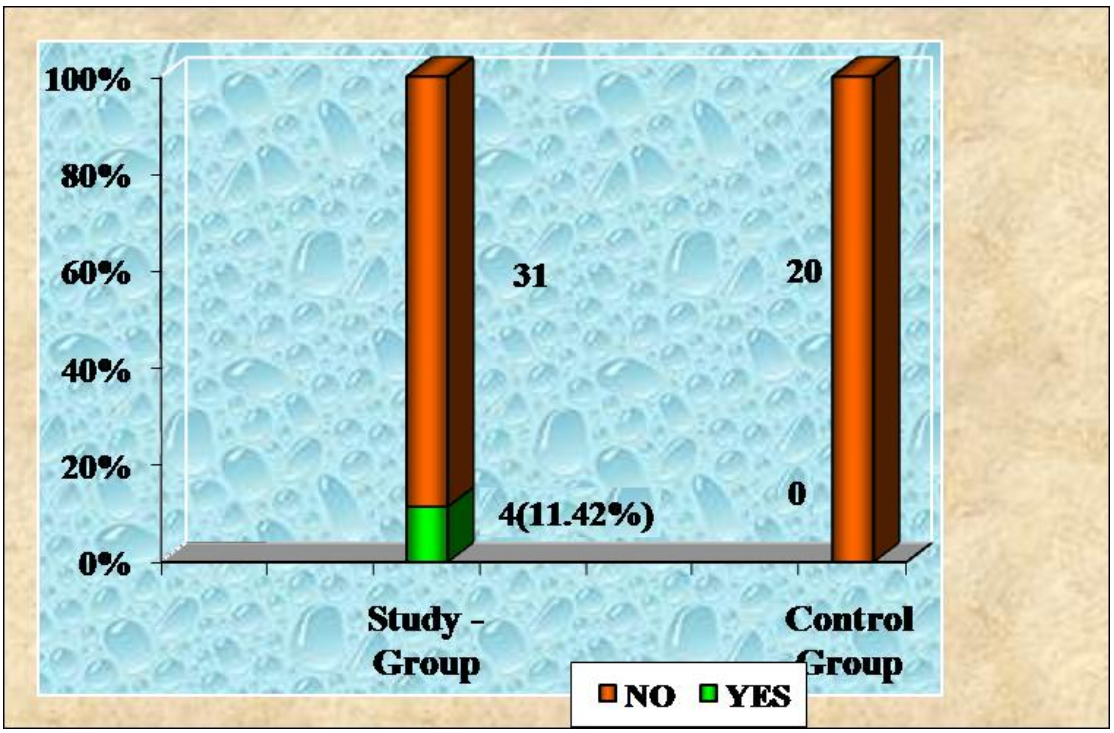


TABLE 10

THYROID AUTOIMMUNITY IN STUDY AND CONTROL POPULATION

Thyroid Autoimmunity	Study group		Control group	
	No	**%**	**No**	**%**
Yes	11	31.4	1	5
No	24	68.6	19	95
'p'	**0.0209 Significant**			

Thyroid autoimmunity which is defined as the presence of Anti TPO Antibodies irrespective of presence of thyroid dysfunction was present in 31.4% of study cases and 5% of control cases. This difference is statistically significant (p = 0.0209).

CHART 10: THYROID AUTOIMMUNITY IN STUDY AND CONTROL POPULATION

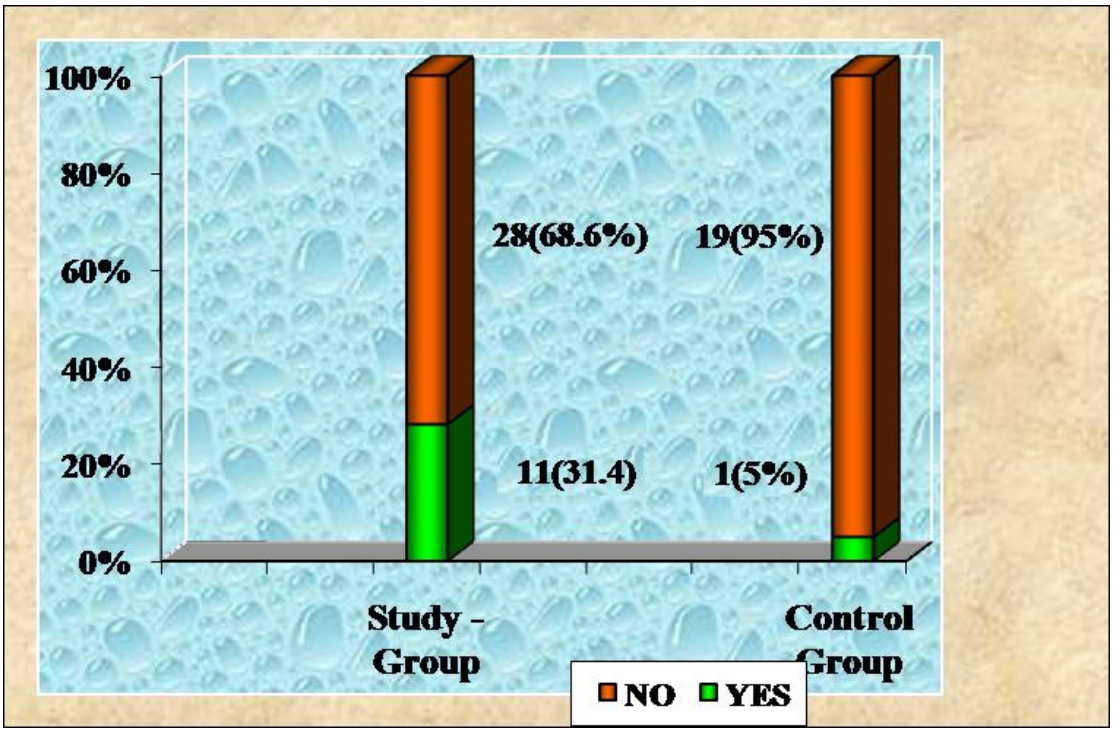


TABLE 11

THYROID AUTOIMMUNITY IN RELATION TO AGE

THYROID AUTOIMMUNITY	Age (in years)	
	Mean	**SD**
Yes	23.0	3.9
No	27.8	8.9
'p'	0.1541 Not significant	

There was no significant relationship between autoimmune thyroiditis and age of the patient.

CHART 11: THYROID AUTOIMMUNITY IN RELATION TO AGE

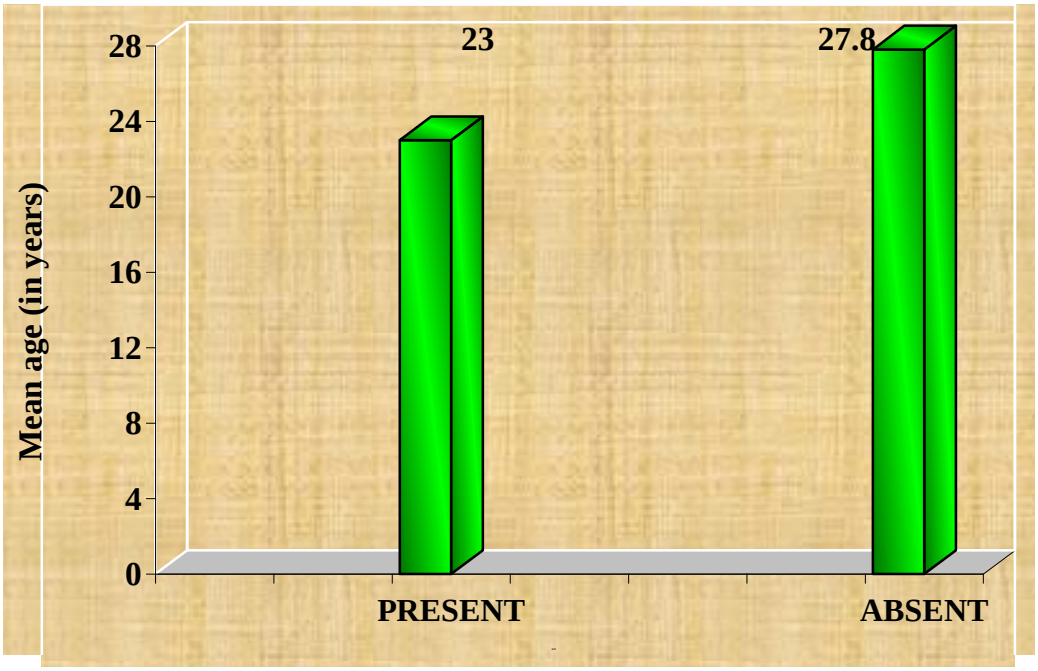


TABLE 12

THYROID AUTOIMMUNITY IN RELATION TO SEX

Sex	No. of cases	THYROID AUTOIMMUNITY			
		Yes		No	
		No	%	No	%
Male	3	-	-	3	100
Female	32	11	34.4	21	65.6
'p'	0.3092 Not significant				

Sex of the patient and incidence of autoimmune thyroiditis were not significantly related ($p > 0.05$).

CHART 12: THYROID AUTOIMMUNITY IN RELATION TO SEX

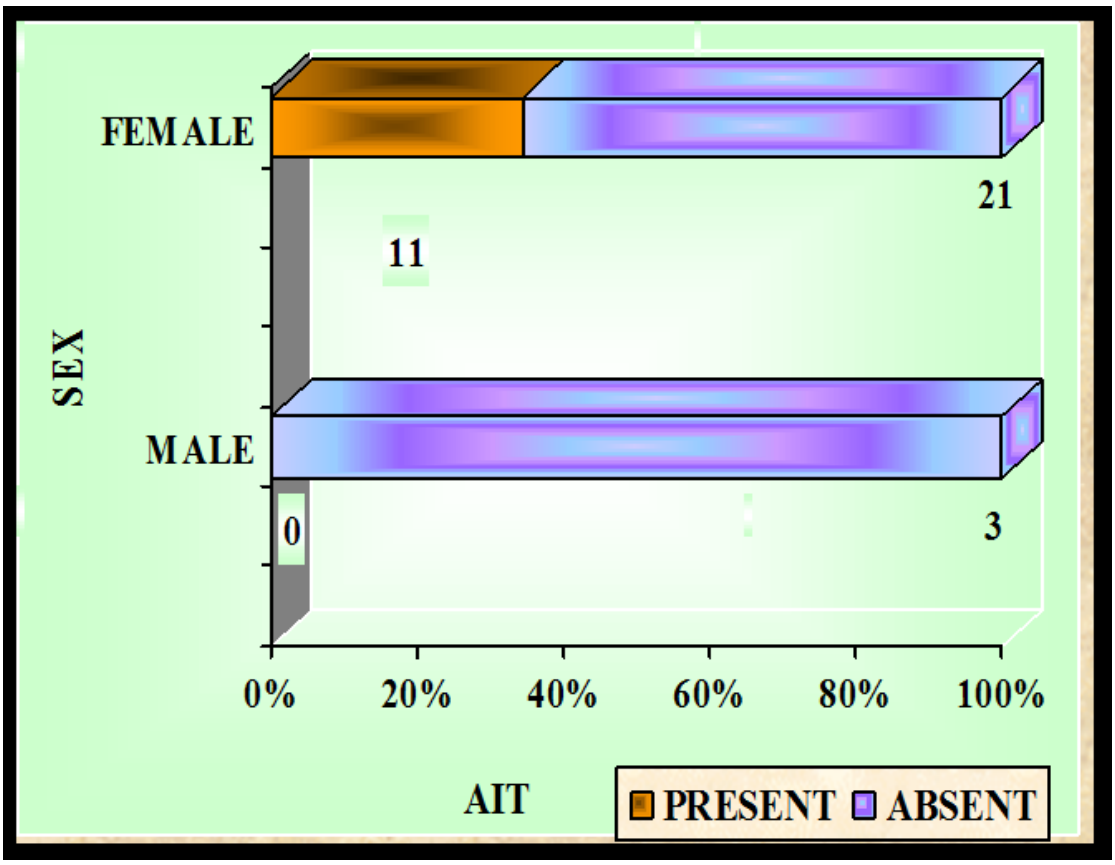


TABLE 13

THYROID AUTOIMMUNITY IN RELATION TO DURATION OF DISEASE

THYROID AUTOIMMUNITY	Duration in years	
	Mean	**SD**
Yes	0.9	1.42
No	1.63	2.28
'p'	0.9425 Not significant	

Duration of illness did not have any significant relationship with incidence of autoimmune thyroiditis.

CHART 13: THYROID AUTOIMMUNITY IN RELATION TO DURATION OF DISEASE

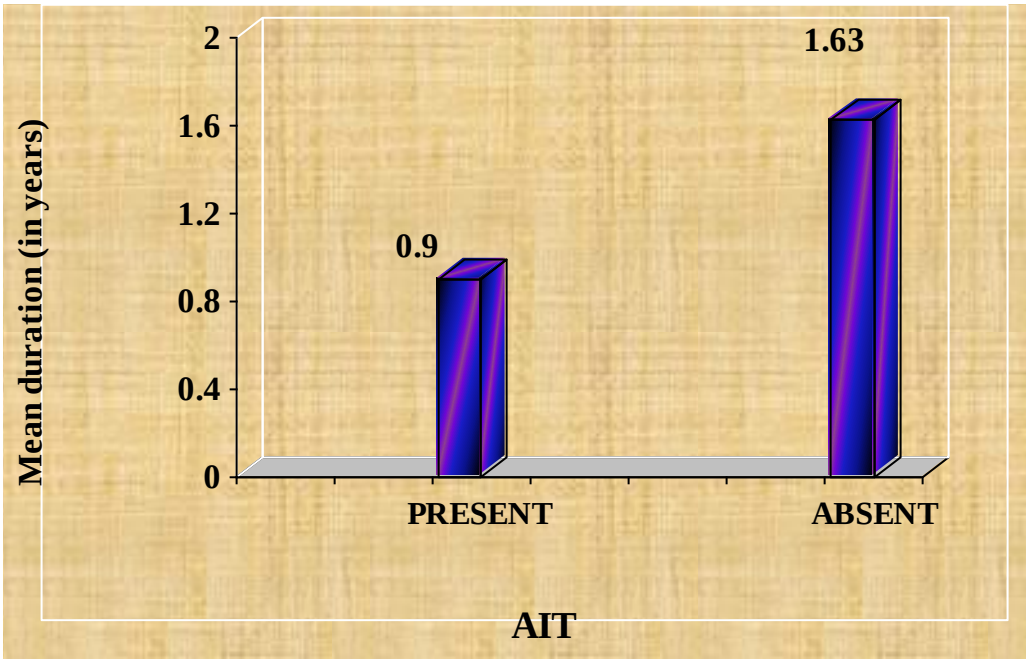


TABLE 14

THYROID AUTOIMMUNITY IN RELATION TO SYMPTOMATOLOGY

Symptoms	**No. of cases**	**THYROID AUTOIMMUNITY**			
		Yes		**No**	
		No	**%**	**No**	**%**
Present	16	6	37.5	10	62.5
Absent	19	5	26.3	14	73.7
'p'	0.7304 Not significant				

Presence or absence of symptoms did not significantly affect the incidence of thyroid autoimmunity ($p = 0.7304$).

TABLE 15

CORRELATION BETWEEN THYROID AUTOIMMUNITY AND THYROID STATUS

Interpretation	No. of cases	Thyroid autoimmunity			
		Yes		No	
		No	%	No	%
Euthyroidism	21	7	33.3	14	66.7
Non thyroidal illness	3	-	-	3	100
Subclinical hypothyroidism	7	3	42.9	4	57.1
Hyperthyroidism	4	1	25	3	75
Total	35	11	31.4	24	68.6

CHART 14: CORRELATION BETWEEN THYROID AUTOIMMUNITY AND THYROID STATUS

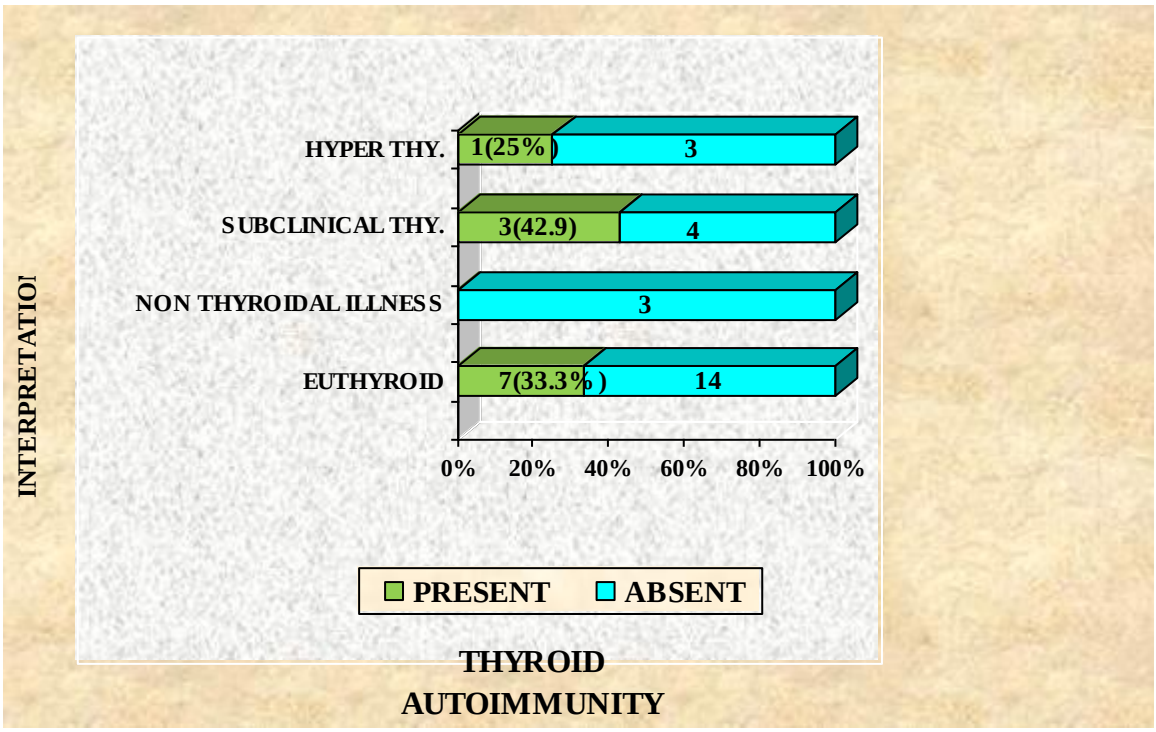


CHART 15 :THYROID AUTOIMMUNITY AND THYROID DYSFUNCTION

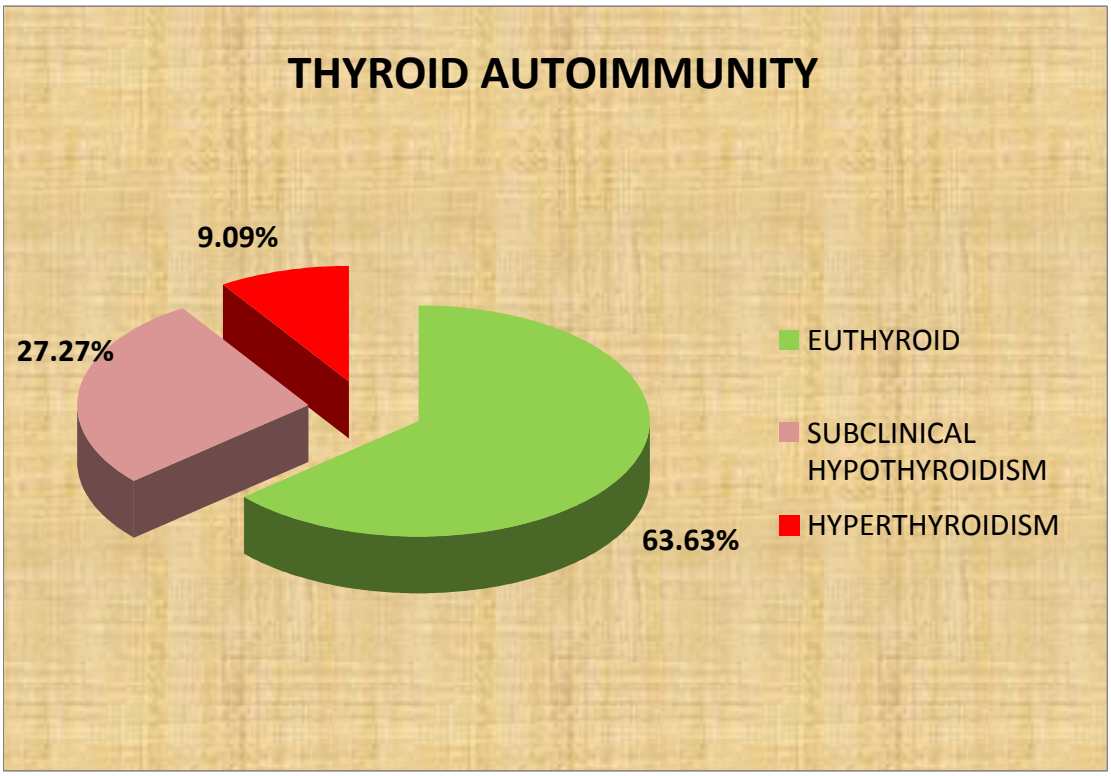


TABLE 16

AUTOIMMUNE THYROID DISEASE IN STUDY AND CONTROL POPULATION

Auto Immune Thyroid Disease	Study group		Control group	
	No	**%**	**No**	**%**
Yes	4	11.42	-	-
No	31	88.57	20	100
'p'	**0.1535 Not Significant**			

Autoimmune thyroid disease defined by the presence of thyroid dysfunction and positive Anti TPO Antibodies was present in 11.42% of the study population as compared to none in the control population. Although there was a higher frequency of AITD in study population as compared to control population, the p value failed to meet statistical significance.

CHART 16: PREVALENCE OF AUTOIMMUNE THYROID DISEASE IN STUDY AND CONTROL GROUP

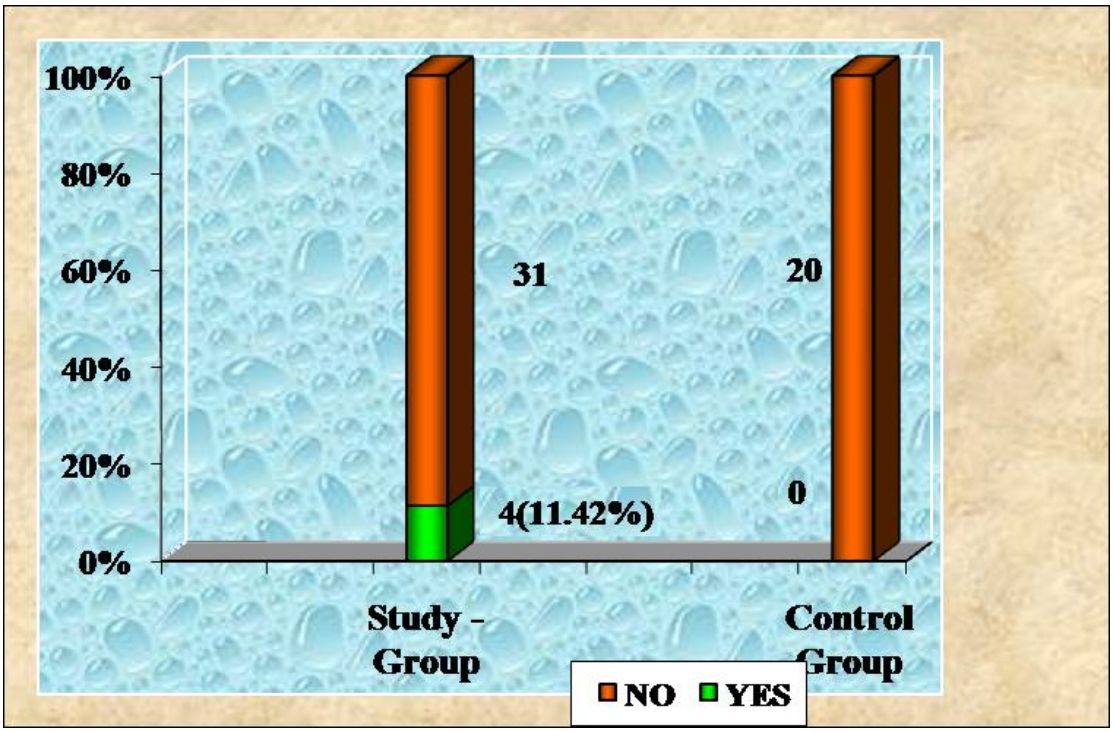


TABLE 17

AUTOIMMUNE THYROID DISEASE AMONG PATIENTS WITH THYROID DYSFUNCTION

THYROID DYSFUNCTION	No. of cases	Thyroid autoimmunity			
		Yes		No	
		No	%	No	%
Subclinical hypothyroidism	7	3	42.85	4	57.1
Hyperthyroidism	4	1	25	3	75
Non thyroidal illness	3	-	-	3	100
Total	14	4	28.57	10	71.42

Among patients with thyroid dysfunction, 28.57 %(4 out of 14) patients were found to have TPO positivity i.e. autoimmune thyroid disease. Out of these 4 patients, 75 %(3 out of 4) had subclinical hypothyroidism and 25 %(1 out of 4) had hyperthyroidism.

CHART 17: AUTOIMMUNE THYROID DISEASE AMONG PATIENTS WITH THYROID DYSFUNCTION

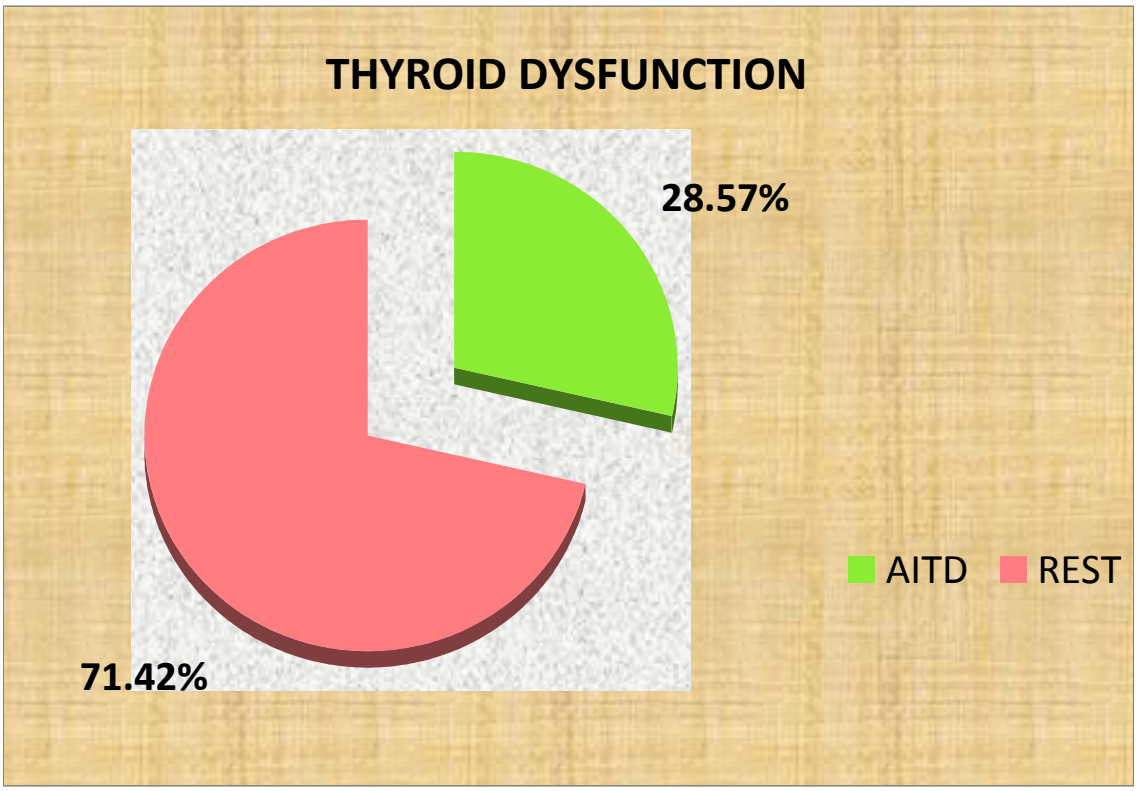
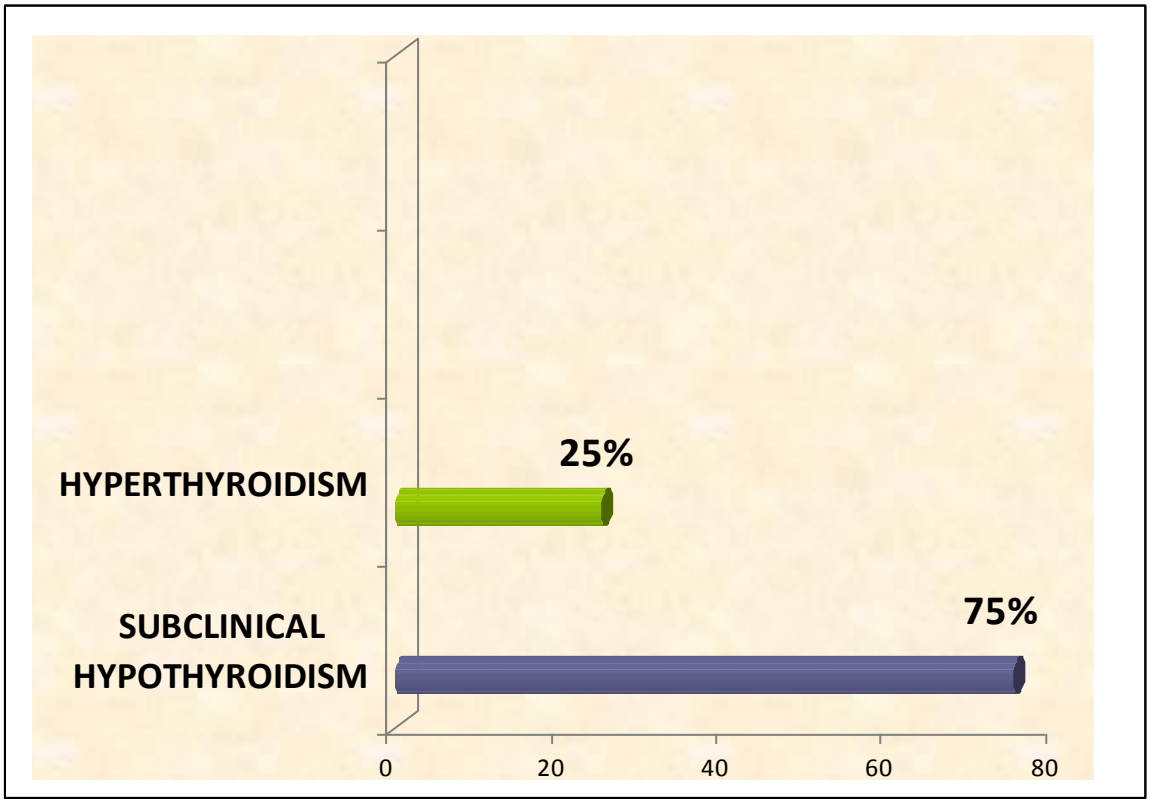


CHART 18: THYROID DYSFUNCTION IN AUTOIMMUNE THYROID DISEASE



OBSERVATIONS

Majority of the patients were from in and around Madurai. The mean age of the study group was 26.3 ±8 years and the control group was 27.7 ±7.9 years. Majority of the patient population were females. 91.4 % of the study group and 85% of the control group were females. Majority of the patients presented with easy fatigability and constitutional symptoms like arthralgias and myalgias. About 45.71% of patients presented with symptomatology suggestive of thyroid dysfunction although there might have been some overlap between rheumatic manifestations. Though the actual numbers are high, there is no statistically significant difference in age, sex and symptomatology, duration of SLE between those with and without thyroid dysfunction.

About 40% of patients from our study group had thyroid dysfunction (20% had subclinical hypothyroidism, 11.4% had hyperthyroidism and 8.6% non thyroidal illness) compared to 5% among the controls. The higher frequency of thyroid dysfunction in SLE population when compared to the control group (40 % vs. 5 %) was found to be statistically significant (p=0.0051). The prevalence of subclinical hypothyroidism (20%) in our study group was higher

than in the control population and met statistical significance (p=0.0331), while that of hyperthyroidism (11.42%) though higher in prevalence failed to meet statistical significance (p=0.1535).The prevalence of thyroid disorders among controls was however found to be of a lesser degree compared to other studies probably due to a smaller sample size[50].

About 31.4% of patients from study group had thyroid autoimmunity (11 out of 35) compared to 5% among the controls. Hence there is a higher prevalence of Anti TPO Ab among SLE patients when compared to controls with statistical significance (p=0.0209). Among these patients, majority were euthyroid (63.63%) followed by subclinical hypothyroidism (27.27%) and the rest hyperthyroid (9.09%).

Combined presence of thyroid dysfunction and Anti TPO Ab positivity defined as autoimmune thyroid disease (AITD) was found at a higher frequency compared with the control group (11.42% vs. 0%), but failed to achieve statistical significance (p=0.1535). Among patients with thyroid dysfunction, the prevalence of AITD was 28.57% out of which subclinical hypothyroidism occurred at a higher frequency compared with hyperthyroidism.

6. DISCUSSION

Several studies have documented an association between systemic lupus erythematosus (SLE) and other individual autoimmune diseases (AID) such as Sjögren's syndrome, autoimmune hemolytic anemia and antiphospholipid syndrome (APS). Patients with SLE might develop other AID that could complicate management of SLE by having an adverse impact on damage scores and mortality[9]. The association of thyroid disorders with SLE has long been the subject of several studies[2, 17, 19, 30-38]. Our study aimed to determine whether the increased frequency with which thyroid abnormalities occurred in SLE patients was more than a chance association.

In our series of 35 patients with SLE, 40% had thyroid dysfunction out of which the prevalence of subclinical hypothyroidism (20%) and hyperthyroidism (11.42%) was much higher than that noted for the normal background population. Euthyroid sick syndrome was found in 8.6% of patients. Thyroid autoimmunity (Anti TPO Ab positivity) was found in 31.4% of patients out of which thyroid dysfunction was present in 36.36%.

The prevalence of autoimmune thyroid disease (11.42%) in our study population though higher than in control group, however failed to meet statistical significance.

A number of studies have looked at the prevalence of thyroid disease in SLE (Table 18).One of the largest studies done looked at the prevalence of thyroid disease in 332 patients with SLE admitted to hospital in the United States during a five year period[37]. The overall prevalence of thyroid disease was 7.5%—6.6% with hypothyroidism and 0.9% with hyperthyroidism—which is much lower than noted in our study.

Our study did not have patients with overt thyroid dysfunction as compared to several studies which have a prevalence rate over a wider range (3%-14%). This could be due to the underlying fact that autoimmune thyroiditis constitutes an evolving process which might later in the course of the disease present as overt hypothyroidism. Subclinical hypothyroidism was found to be much higher in frequency, probably reflecting the slow destructive process which is pathognomic of autoimmune thyroiditis.

TABLE 18

PREVALENCE OF THYROID DISEASE IN SLE POPULATION

Study	No of cases	Hypo thyroidism (%)	Subclinical Hypothyroidism (%)	Hyper thyroidism (%)	Subclinical hyperthyroidism (%)	ESS (%)
Miller et al[37]	332	6.6	-	0.9	-	-
Pyne et al[30]	300	5.7	-	1.7	-	-
Gao et al[42]	1006	1.69	10.04	1.19	-	9.54
Kumar et al[41]	100	14	12	-	2	8
Chan et al[40]	69	4.3	13	2.9	2.9	1.5
Park et al[45]	61	9.5	-	4.8	-	14.3
Boey et al[34]	129	3.9	-	8.9	-	47.8
El-Sherif WT et al[48]	20	10	10	5	5	20
Appenzeller et al[46]	524	-	11.5	-	-	-
PRESENT STUDY	35	-	20	11.42	-	8.6

Pyne et al[30] had conducted a retrospective analysis of 300 SLE cases, wherein the prevalence of overt hypothyroidism was higher than in our study group (5.7% vs.0%), while the prevalence of hyperthyroidism was lower (1.7% vs.11.42%). Anti TPO Ab

positivity was found in 14% and there was no significant difference in the frequency with which antimicrosomal antibodies were detected between the hyperthyroid and hypothyroid subgroups. On the contrary, our study revealed a higher prevalence of subclinical hypothyroidism and antimicrosomal antibodies.

Our study showed the prevalence of subclinical hypothyroidism (20%) to be higher than that of the control group. Our findings are similar to a large retrospective cohort study done in Chinese patients which also had higher prevalence of subclinical hypothyroidism (10.04%) compared to other causes of thyroid dysfunction[42]. Subclinical hypothyroidism was found to be more associated with lupus nephritis. Our conclusions are also supported by similar studies done by Kumar et al[41] and Chan et al[40] which also showed the prevalence of subclinical hypothyroidism to be higher than that of overt hypothyroidism.

Few data are available regarding the association of SLE with hyperthyroidism[39]. The prevalence of hyperthyroidism in our patients with SLE was 11.42% comparable to 8.9% in a study conducted by Boey et al[34]. There are also several case reports associating Graves's disease with SLE but further studies are needed

for confirmation of the above association. The prevalence of sick euthyroid syndrome also matched the prevalence rates in similar studies.

Several recent studies have addressed the question of whether antithyroid antibodies (especially Anti TPO Ab) are present in patients with SLE (Table 19). The prevalence of Anti TPO Ab in our study group was 31.4% comparable to 32.2%, 46.7%, and 31% in studies conducted by Boey et al[34], Tsai et al[33] and Ebernard et al[36] respectively. An association was also noted between the activity of the disease with the presence of antithyroid antibodies[44]. Thyroid autoantibodies preceded the occurrence of clinical autoimmune thyroid disease in 70% of SLE patients[46]. Antithyroid autoantibodies may be good predictors for the detection of Hashimoto's thyroiditis developing in SLE[45].

TABLE 19

PREVALENCE OF THYROID DYSFUNCTION/

ANTI TPO Ab /AITD IN SLE PATIENTS

Study	No of cases	Anti thyroid Ab (%)	AITD (%)	Thyroid dysfunction (%)
Kumar et al[41]	100	30	18	36
Pyne et al[30]	300	14	-	7
Gao et al[42]	1006	-	2.78	25
Chan et al[40]	69	23.2	20.3	24.6
Weetman et al[32]	41	51	24.39	-
Park et al[45]	61	27	14.3	-
Appenzeller[46]	524	-	6.1	-
Present study	35	31.4	11.42	40

Weetman et al[32] compared the prevalence of thyroid autoantibodies and abnormal thyroid-stimulating hormone (TSH) levels in 41 SLE patients with age- and sex-matched controls. Twenty-one (51%) of the SLE patients had thyroid antibodies compared to 11(27%) controls ($p<0.05$). Ten SLE patients and five

controls had elevated TSH levels, usually in association with the presence of thyroid autoantibodies. These results suggest that SLE is associated with autoimmune thyroiditis and that many patients with SLE have minor hypothyroidism, which further supports the results of our study.

The prevalence of autoimmune thyroid disease in our study group was 11.42% which is also similar to previous studies (table 19), although the difference failed to meet statistical significance. Hypothyroidism was the predominant manifestation similar to that seen in a study by Appenzeller et al[45].

Although many international studies have been done, there are very few studies to be validated with, in India. In a study conducted by Kumar K et al[41] 36% of patients were found to have thyroid dysfunction when compared to 8% of controls which was similar to our study (40%). All patients were women as against a small percentage (18.18%) of males in our study. Disease duration and symptomtomatology had no significant correlation with thyroid dysfunction or thyroid autoimmunity. Primary hypothyroidism was the commonest dysfunction(14%) whereas our study revealed subclinical hypothyroidism was more common(20%).The prevalence

of thyroid autoimmunity(30% vs.31.4%) and autoimmune thyroid disease (18% vs.11.4%)were similar in both the studies. However, among the patients with thyroid disease equal prevalence of both autoimmune (50%) and non autoimmune disease (50%) were found whereas our study showed the prevalence of AITD to be 28.57%. So our study conclusions are almost similar except for the higher prevalence of subclinical hypothyroidism.

Pregnant women with SLE will have a high prevalence of undiagnosed hypothyroidism and a high prevalence of postpartum thyroiditis and women with SLE and thyroid disease will have an increased incidence of adverse pregnancy outcomes as compared with pregnant women with SLE who do not have thyroid disease. The prevalence of preterm delivery was 67% in women with thyroid disease and 18% in women who were thyroid disease free[43]. Hence the need for appropriate screening tests in SLE population and treatment if required.

Hence, screening for autoimmune thyroid diseases should be recommended in everyday clinical practice, in patients with primary organ-specific or organ non-specific autoimmune disease. Patients with SLE have a higher prevalence of significantly more subclinical

hypothyroidism and positive thyroid autoantibodies[46, 48]. Thyroid autoantibodies may precede the appearance of clinical autoimmune disease. Since symptoms of SLE and thyroid disease can be similar, SLE patients should routinely been investigated for autoimmune thyroid disease[46]. Subjects at high risk (women, positive Ab TPOs) should have thyroid function follow-up and appropriate treatment in due course[47].

7. CONCLUSION

- SLE was associated with significant thyroid dysfunction and autoimmunity when compared with the normal population

- The prevalence of subclinical hypothyroidism was much higher than that of overt hypothyroidism, thus making the clinical diagnosis difficult.

- There is a higher frequency of occurrence of hyperthyroidism and sick euthyroid syndrome in SLE compared to general population though not statistically significant.

- Presence of Anti Thyroid Peroxidase antibodies was more in SLE patients suggesting an ongoing destructive autoimmune thyroiditis which may later manifest as overt or subclinical hypothyroidism

- Gender, age and duration of SLE may or may not have a significant association with thyroid autoimmunity.

In summary, polyautoimmunity is frequent in SLE, and it is influenced by clinical and immunological features. Systemic and thyroid autoimmune diseases often overlap with each other. Therefore it is clinically important to screen patients with systemic autoimmune diseases for the co-existence of thyroid disorders. Patients with co-existing thyroid disease and SLE may escape clinical detection because of overlapping clinical features. Hence serological testing for autoimmune thyroid disease and appropriate treatment is warranted in this subset of patients for better quality of life.

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9. PROFORMA

NAME : IP NO :

AGE : SEX :

ADDRESS :

KNOWN CASE / NEWLY DETECTED CASE OF SLE

HISTORY :

- Easy fatigability
- Cold intolerance/ heat intolerance
- Constipation / diarrhea
- Weight gain / weight loss
- Hair loss
- Difficulty concentrating and poor memory
- Breathing difficulty
- Hoarse voice
- Menstrual abnormalities
- Impaired hearing

OTHER SYMPTOMS OF RELEVANCE

PAST HISTORY:

Hypertension / coronary heart disease / Hypothyroidism

Surgery / irradiation / drug intake

Chronic kidney disease

FAMILY HISTORY

TREATMENT HISTORY:

Duration of SLE TREATMENT:

EXAMINATION

GENERAL EXAMINATION

Build / Nourishment

Waist: hip ratio:

BMI: Ht: Wt:

Temperature

Pallor

Clubbing

Lymphadenopathy

Pedal edema

Hydration

Features of hypothyroid / hyperthyroidism:

Ophthalmology examination:

Skin changes

Thyroid:

BP: PR: RR:

PER ABDOMEN:

Soft / rigid / Tender / non tender

Distended

Organomegaly

Bowel sounds / Bruit

CARDIOVASCULAR SYSTEM:

Heart sounds / Murmurs

RESPIRATORY SYSTEM:

Breath sounds / Added sounds

CNS

Tremors

Evidence of peripheral neuropathy

Focal neurological deficit

OTHER FINDINGS:

INVESTIGATIONS:

1. TC, DC, Hb
2. Sugar, urea, creatinine
3. T3, T4, TSH.
4. Urine routine.
5. Anti TPO Ab

OTHER RELEVANT INVESTIGATIONS

MASTER CHART

NO	AGE	SEX	DURATION	SYMPTOMS	T3	T4	TSH	TPO	INTERPRETATION	AUTOIMMUNE THYROIDITIS
1	30	F	NEW	PRESENT	1.6	128.1	6.3	9.89	SUBCLINICAL HYPOTHYROIDISM	----
2	29	F	5 YEARS	PRESENT	1.1	83.4	7.4	114.60	SUBCLINICAL HYPOTHYROIDISM	+
3	24	F	6 MONTHS	ABSENT	4.8	188.6	0.04	35.91	HYPERTHYROIDISM	+
4	28	F	NEW	PRESENT	1.3	126.3	0.9	7.63	EUTHYROID	-----
5	24	F	7 YEARS	ABSENT	1.2	60.8	2	16.34	EUTHYROID	-----
6	52	F	6 MONTHS	ABSENT	1.7	112.30	1.58	31.88	EUTHYROID	-----
7	22	M	3 YEARS	ABSENT	0.8	109.74	5.47	12.29	SUBCLINICAL HYPOTHYROIDISM	-----
8	24	F	NEW	ABSENT	1.2	123.45	17.71	72.60	SUBCLINICAL HYPOTHYROIDISM	+
9	33	F	4 MONTHS	PRESENT	0.8	102.41	3.47	17.68	EUTHYROID	-----
10	22	F	1 MONTH	PRESENT	3	177.1	0.02	27.14	HYPERTHYROIDISM	-----
11	39	F	6 MONTHS	PRESENT	2.3	83.8	0.34	13.8	HYPERTHYROIDISM (T3)	-----

12	32	F	1 YEAR	PRESENT	1.1	102.0	2.1	17.21	EUTHYROID	-----
13	30	F	1 YEAR	PRESENT	0.9	88.7	2.7	67.78	EUTHYROID	+
14	23	F	4 YEARS	ABSENT	1.2	130.4	1.6	19.59	EUTHYROID	-----
15	21	F	1 YEAR	ABSENT	0.9	83.8	1	86.21	EUTHYROID	+
16	20	F	2 YEARS	ABSENT	0.8	67	2.6	11.18	EUTHYROID	-----
17	23	F	2 MONTHS	PRESENT	0.8	100.3	3.09	338.90	EUTHYROID	+
18	35	F	NEW	ABSENT	1.05	102	1.02	12.51	EUTHYROID	------
19	36	F	6 MONTHS	ABSENT	2	129	1	18.26	EUTHYROID	-----
20	19	F	4 YEARS	ABSENT	1.3	211	0.09	28.82	HYPERTHYROIDISM (T4)	-----
21	19	F	1 YEAR	PRESENT	1.7	118	0.7	76.03	EUTHYROID	+
22	24	F	6 MONTHS	PRESENT	1.6	91	3.1	145.3	EUTHYROID	+
23	21	F	NEW	PRESENT	1.2	99	6.3	24.58	SUBCLINICAL HYPOTHYROIDISM	----
24	23	F	NEW	ABSENT	0.9	107	1.6	13	EUTHYROID	------
25	16	M	3 MONTHS	PRESENT	1	120	6.2	18	SUBCLINICAL HYPOTHYROIDISM	------
26	45	F	8 YEARS	ABSENT	0.53	80.4	1.87	14.49	**NON THYROIDAL ILLNESS**	----
27	17	F	1 MONTH	PRESENT	1.6	122.60	3.54	349.40	EUTHYROID	+

28	21	F	NEW	PRESENT	0.9	85.9	3.76	25.25	EUTHYROID	-----
29	17	M	2 YEARS	ABSENT	0.6	109.1	0.741	26.17	**NON THYROIDAL ILLNESS**	-----
30	24	F	NEW	ABSENT	0.48	59.1	3.51	13.67	**NON THYROIDAL ILLNESS**	------
31	26	F	NEW	PRESENT	0.9	62.80	2	24.60	EUTHYROID	------
32	32	F	4 YEARS	ABSENT	1.1	122.40	3.2	18.78	EUTHYROID	------
33	22	F	8 MONTHS	ABSENT	1.7	92.33	1.6	56.72	EUTHYROID	+
34	26	F	2 YEARS	ABSENT	1.6	110.58	0.8	12.68	EUTHYROID	------
35	20	F	NEW	ABSENT	1.7	95.3	19.20	600	SUBCLINICAL HYPOTHYROIDISM	+

AGE AND SEX MATCHED CONTROLS

NO	AGE	SEX	T3	T4	TSH	TPO	INTERPRETATION	AUTOIMMUNE DISEASE
1	15	M	1.4	92.1	2.08	22.59	EUTHYROID	--
2	18	M	1.6	108.2	3.45	32.24	EUTHYROID	--
3	18	M	1.2	102.4	3.35	11.67	EUTHYROID	--
4	38	F	1.16	69.5	3.65	18.49	EUTHYROID	--
5	34	F	1.54	102.4	5.10	10.66	EUTHYROID	--
6	16	F	1.12	75.8	1.77	75.58	EUTHYROID	+
7	29	F	1.4	96.3	2.12	9.82	EUTHYROID	--
8	35	F	1.02	89.8	1.53	12.29	EUTHYROID	--
9	30	F	0.42	104.6	7.84	31.22	NON THYROID ILLNESS	--
10	30	F	1.56	90.9	3.45	33.48	EUTHYROID	--

11	40	F	1.32	106	2.75	28.22	EUTHYROID	--
12	35	F	1.2	96.40	3.10	24.78	EUTHYROID	--
13	15	F	0.96	109.8	3.31	8.23	EUTHYROID	--
14	27	F	1.43	115.6	3.71	6.13	EUTHYROID	--
15	26	F	1.2	76.9	4.23	8.29	EUTHYROID	--
16	32	F	1.21	83	2.05	9.05	EUTHYROID	--
17	32	F	0.9	91	2.81	5.62	EUTHYROID	--
18	28	F	1.6	126.86	2.64	11.34	EUTHYROID	--
19	34	F	1.4	110.24	3.18	21.34	EUTHYROID	--
20	22	F	1.2	76.20	1.54	8.82	EUTHYROID	--